

**REMARKS/ARGUMENTS**

Claims 49-53, 56, 57, 60, 61, 63-71, 75, 76, 79, 80, 82, 83, 86-91, 94, 95, 98, 99, 101, 105-113 and 120-148 are pending in the present application. Claims 49, 64, 86, and 125-127 have been amended. Claims 60-61, 79-80, 83, 98-99, 128-129, 135-136 and 142-143 have been canceled. Reconsideration of the present application is respectfully requested in light of the foregoing amendments and following remarks.

**I. Claim Rejections - 35 USC § 102**

Claims 49, 64, 67-71, 80, 86, 126-127, 129, 136 and 143 have been rejected under 35 U.S.C. 102(b) as allegedly being anticipated by U.S. Patent No. 4,665,192 to Cerami, ("Cerami"). The Examiner alleges that Cerami teaches a mass spectrometry apparatus using a ceramic probe tip to present the sample. In order to further the prosecution of the application, Applicants have amended claims 49, 64, 86, without acquiescence and prejudice as set forth above. In addition, Applicants have canceled claims 61, 80, 99, 129, 136 and 143. Applicants respectfully submit that amended claims 49, 64 and 86 overcome the section 102(b) rejections because the Cerami reference does not teach all the elements of the amended claims. Furthermore, considering that claims 67-71, 80, 126 and 136 include all of the features and limitations of amended independent claim 64 from which they depend, these claims are patentable to the same extent that amended independent claim 64 is patentable. In addition, considering that claims 127 and 143, include all of the features and limitations of amended independent claim 86 from which they depends, these claim are also patentable to the same extent that amended independent claim 86 is patentable.

**II. Claim Rejections - 35 USC 103 - DE 3221681 or Cottrell et al.**

Claims 49-50, 52, 56-57, 63-67, 69-71, 75-76, 82, 86-87, 90-91, 94-95, 101, 105-127, 130-134, 137-141 and 144-148 have been rejected under 35 U.S.C. 103(a) as allegedly being obvious over DE 3221681 or U.S. Patent No. 5,260,571 to Cottrell et al. ("Cottrell"). Applicants respectfully disagree and traverse this rejection for reasons set forth below.

According to the Examiner, DE 3221681 "teaches a method and apparatus for using a laser to desorb a biological sample from a polymer film further subjecting the desorbed sample to mass spectrometry analysis." The Office Action provides that "DE 3221681 is silent to the type of polymer used and if the material is open or closed pore." The Office Action later states that, " it would have been within the skill of the art to modify DE 3221681 and use polymeric materials such as polystyrene, polypropylene, polycarbonate, nylon and dextran as well as selecting the relative porosity to gain the above advantages and as selection of material based upon its suitability of intended use."

While Applicants agree with the Examiner in that DE 3221681 is silent to the type of polymer used and if the material is open or closed pore, Applicants respectfully disagree with the Examiner's apparent understanding of the DE 3221681 reference. A review of the DE 3221681 reference shows that the thin polymer film disclosed therein, which is used to present a sample, is one part of a two piece assembly, which relies on a separate large metallic sample holder. In stark contrast, the probe in accordance with the embodiments of the present invention is one-piece unitary device, where at least the surface comprises a non-metallic-material selected from the group consisting of polystyrene, polypropylene, polyethylene, polycarbonate, nylon, starch, agarose, and dextran, and wherein the probe for presenting the analyte is not associated with a separate sample holder. The DE 3221681 reference is completely silent with regard to such a one-piece or unitary construction. In fact, the polymer film of the DE 3221681 reference needs the separate large metallic member for both structural and functional support, while the probe of the presently claimed invention does not require such a separate structural member. Applicants have amended claims 49, 64, 86, without acquiescence and prejudice as set forth above, and Applicants respectfully submit that the claims as amended are patentable over the DE 3221681 reference for reasons set forth above.

In addition, a review of the DE 3221681 reference shows that the thin polymer film disclosed therein is placed outside of a mass spectrometer. For example see page 2 , lines 3-4, where the English translation provides: " ... sample fixed on a thin polymer foil being placed outside of the mass spectrometer...". The teachings of the DE 3221681 reference are motivated

by keeping the sample presenting surface out of the mass spectrometer chamber. Clearly, this reference teaches away from having a system and a method where a mass spectrometer probe is removably inserted into a mass spectrometer as is set forth by the claims currently under examination. Assuming arguendo that a motivation did exist, which does not, to modify the DE 3221681 reference to use polymeric materials such as those set forth by the presently claimed invention, the hypothetical combination would still not render the claimed invention obvious, because as is taught by the DE 3221681 reference, the polymeric film would have to be supported by a separate sample holder and the polymeric film would have to be placed on the outside of a mass spectrometer, whereas the presently claimed invention is directed to a system and a method where a mass spectrometer probe is removably inserted into a mass spectrometer and where the probe in accordance with the embodiments of the present invention is one-piece unitary device. For reasons set forth above, Applicants respectfully submit that the rejection is improper and hence the withdrawal of the rejection is respectfully requested.

Turning next to the Cottrell reference, the Office Action alleges that: "Cottrell et al. teach a method and apparatus for laser desorption mass spectrometry of a sample on a polyacrylamide gel." The Office Action also provides that: "Cottrell et al. is silent to the claimed polymers and if the material is open or closed pore." While the Applicants agree in that Cottrell is silent to the claimed polymers and if the material is open or closed pore, Applicants respectfully disagree with the remainder of the assessment of the Cottrell reference. The Cottrell reference does not teach a method and a system where a probe that is removably insertable into a mass spectrometer where the probe has a surface for presenting the macromolecular analyte, and where the surface comprises a non-metallic material selected from the group consisting of polystyrene, polypropylene, polyethylene, polycarbonate, nylon, starch, agarose, and dextran, as is presently claimed.

A review of col. 3, line 25-40 of Cottrell indicates that the polyacrylamide gel as disclosed in Cottrell is not placed on a mass spectrometer probe that is later placed in a mass spectrometer. The polyacrylamide gel as disclosed in Cottrell is placed in a semi-dry blotting tank on a filter paper. The setup of the blotting tank with the polyacrylamide gel as shown in

Fig. 2 of Cottrell is used, as an alternate method to that described in Fig.1 of Cottrell, to induce proteins to migrate from the polyacrylamide gel towards a substrate material where they are bound. The target substrate is then removed from the blotting tank with the polyacrylamide gel, rinsed, matrix solution added, dried and introduced into the source region of a mass spectrometer, as set forth in col. 4, lines 1-5 of Cottrell. For reasons set forth above, Cottrell does not teach that its polyacrylamide gel is placed on a mass spectrometer probe that is later placed in a mass spectrometer. Assuming arguendo that a motivation did exist, which does not, to modify Cottrell to use polymeric materials such as those set forth by the presently claimed invention, the hypothetical combination would still not render the claimed invention obvious, because as is taught by the Cottrell reference, the polymeric film would have to be placed in a blotting tank to transfer proteins towards a substrate material where they are bound, whereas the presently claimed invention is directed to a method and a system where a probe that is removably insertable into a mass spectrometer where the probe has a surface for presenting the macromolecular analyte, and where the surface comprises a non-metallic material selected from the group consisting of polystyrene, polypropylene, polyethylene, polycarbonate, nylon, starch, agarose, and dextran. Accordingly, Applicants respectfully submit that the rejection of the presently pending claims based on the Cottrell reference is improper and hence the withdrawal of the rejection is respectfully requested.

**Claim Rejections - 35 USC 103 - Cerami in view of Stuke**

Dependent claims 50, 52, 56-57, 60-61, 63, 75-79, 82-83, 87-99, 101, 105-125, 128-129, 135 and 142 have been rejected under 35 U.S.C. 103(a) as allegedly being obvious over Cerami in view of U.S. Patent No. 4,686,366 to Stuke ("Stuke"). The Office Action states that Cerami teaches a mass spectrometry apparatus using a ceramic probe tip to present the sample, as set forth above; and that Cerami is silent to the claimed use of glass and their relative porosity of either the taught ceramic or glass. The Office Action alleges that Stuke teaches that it is advantageous to use a laser to desorb the sample to supply the mass spectrometer with large intact analytes. The Examiner alleges it would have been within the skill of the art to modify

Cerami in view of Stuke and use a laser to desorb the sample. The Examiner also alleges that it would have been within the skill of the art to use other well-known silicon based materials such as glass and that allegedly it would have been within the skill of the art to modify Cerami in view of Stuke and use glass instead of the taught ceramic as well as selecting the relative porosity to gain advantages and as selection of a material based upon its suitability of intended use.

Applicants have amended independent claims 49, 64 and 86 as set forth above. In addition, Applicants have canceled claims 60, 79, 83, 98, 128, 135 and 142. Neither Cermai, nor Stuke, nor a putative combination of Cerami and Stuke teach or suggest all of the limitations of independent claims 49, 64 or 86. In particular neither Cerami, nor Stuke, nor a putative combination of Cerami and Stuke teach a method and a system where a probe that is removably insertable into a mass spectrometer has a surface for presenting the macromolecular analyte, and where the surface comprises a non-metallic material selected from the group consisting of polystyrene, polypropylene, polyethylene, polycarbonate, nylon, starch, agarose, and dextran, and where the surface of the probe for presenting the analyte is not associated with a separate sample holder. Applicants respectfully submit that for reasons set forth above, amended independent claims 49, 64 and 86 are not obvious over Cerami in view of Stuke. Furthermore, considering that claims 50, 52, 56-57, 61, 63, 105-107, 120 and 125 include all of the features and limitations of amended independent claim 49 from which they depend, these claims are patentable to the same extent that amended independent claim 49 is patentable.

In addition, considering that claims 75-78, 82, 108-110, 121-122 include all of the features and limitations of amended independent claim 64 from which they depend, these claims are patentable to the same extent that amended independent claim 64 is patentable.

And further, considering that claims 87-99, 101, 111, and 123-124 include all of the features and limitations of amended independent claim 86 from which they depend, these claims are patentable to the same extent that amended independent claim 86 is patentable.

**III. Allowable Subject Matter**

Claims 51, 53, 88 and 89 have been objected to as being dependent upon a rejected base claim, but are allowable if rewritten in independent from including all of the limitations of their bases claim and any intervening claims. Applicants are pleased that the Examiner has found these claims allowable. However, Applicants respectfully submit that claims 51, 53, 88 and 89 are allowable even if they are not rewritten as suggested above in view of the above amendments of their base claims and reasons set forth above.

**CONCLUSION**

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 925-472-5000.

Respectfully submitted,



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